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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,794	06/08/2001	Suzanne A. W. Fuqua	UTSK:348US/MBW	5270

7590 06/30/2003

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EXAMINER	
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ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/877,794	Applicant(s) Fuqua et al
	Examiner Ungar	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *one* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 25, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☐ Claim(s) _____ is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-21* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The Election filed February 25, 2003 (Paper No.11) in response to the Office Action of September 19, 2002 (Paper No. 7) is acknowledged and has been entered. Applicant has provisionally elected the invention of Group 1, claim 1 drawn to *in vitro* detection of tamoxifen-resistant breast cancer cells, provisionally electing the species of utilizing an antibody that specifically binds to tyrosine protein kinase receptor (TIE-2). It is noted that Examiner specifically stated that the invention drawn specific antigens are not species elections and that they are drawn to separate and distinct inventions. In order to clarify the record and the restriction requirement which Applicant states is duplicative and indistinct, the prior restriction requirement is hereby withdrawn.

2. Upon review and reconsideration, Restriction to one of the following inventions is required under 35 U.S.C. § 121:

3. It is noted that claim 1 drawn to TIE-2 of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 1. Claims 1,3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with antibody binding to TIE-2, classified in Class 435, subclass 7.1

Group 2-64. Claims 1-3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells comprising assaying an obtained sample with antibody binding to TIE-2 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TIE-2 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 65. Claims 1,3 and 4 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of TIE-2 in an

immunoassay, in an obtained sample, with antibody binding to TIE-2, classified in Class 435, subclass 7.1

Group 66-129. Claims 1-3 and 4, as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of TIE-2 in an immunoassay, in an obtained sample, with antibody binding to TIE-2 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TIE-2 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 130. Claims 1,3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting TIE-2, comprising assaying an obtained sample with antibody binding to TIE-2, classified in Class 435, subclass 7.1

Group 131--194. Claims 1-3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting TIE-2, comprising assaying an obtained sample with antibody binding to TIE-2 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TIE-2

must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

4. It is noted that claim 1 drawn to EDNRA of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 195. Claims 1,3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer

comprising assaying an obtained sample with antibody binding to EDNRA, classified in Class 435, subclass 7.1

Group 196-259. Claims 1-3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells comprising assaying an obtained sample with antibody binding to EDNRA and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein EDNRA must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 260. Claims 1,3 and 4 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of EDNRA in an immunoassay, in an obtained sample, with antibody binding to EDNRA, classified in Class 435, subclass 7.1

Group 261-324. Claims 1-3 and 4, as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of EDNRA in an immunoassay, in an obtained sample, with antibody binding to EDNRA and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial

expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein EDNRA must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 325. Claims 1,3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting EDNRA, comprising assaying an obtained sample with antibody binding to EDNRA, classified in Class 435, subclass 7.1

Group 136–389. Claims 1-3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting EDNRA, comprising assaying an obtained sample with antibody binding to EDNRA and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein EDNRA must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

5. It is noted that claim 1 drawn to TGF beta 3 of the instant application has been determined to be a linking claim. The restriction requirement among the linked

inventions is subject to the nonallowance of the linking claim(s), claims 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 195. Claims 1,3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with antibody binding to TGF beta 3 , classified in Class 435, subclass 7.1

Group 196-259. Claims 1-3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells comprising assaying an obtained sample with antibody binding to TGF beta 3 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1}

or 2^6 in the instant case, the number of possible combinations, wherein TGF beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 260. Claims 1,3 and 4 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of TGF beta 3 in an immunoassay, in an obtained sample, with antibody binding to TGF beta 3, classified in Class 435, subclass 7.1

Group 261-324. Claims 1-3 and 4, as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of TGF beta 3 in an immunoassay, in an obtained sample, with antibody binding to TGF beta 3 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGF beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 325. Claims 1,3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting TGF beta 3,

comprising assaying an obtained sample with antibody binding to TGF beta 3, classified in Class 435, subclass 7.1

Group 136–389. Claims 1-3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting TGF beta 3, comprising assaying an obtained sample with antibody binding to TGF beta 3 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGF beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

6. It is noted that claim 1 drawn to TGFR beta 3 of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or

nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 390. Claims 1,3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with antibody binding to TGFR beta 3 , classified in Class 435, subclass 7.1

Group 391-454. Claims 1-3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells comprising assaying an obtained sample with antibody binding to TGFR beta 3 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGFR beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 455. Claims 1,3 and 4 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of TGFR beta 3 in

an immunoassay, in an obtained sample, with antibody binding to TGFR beta 3, classified in Class 435, subclass 7.1

Group 456-519. Claims 1-3 and 4, as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of TGFR beta 3 in an immunoassay, in an obtained sample, with antibody binding to TGFR beta 3 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGFR beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 520. Claims 1,3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting TGFR beta 3, comprising assaying an obtained sample with antibody binding to TGFR beta 3, classified in Class 435, subclass 7.1

Group 521-584. Claims 1-3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting TGFR beta 3, comprising assaying an obtained sample with antibody binding to TGFR beta 3 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible

combinations, wherein TGFR beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

7. It is noted that claim 1 drawn to VEGFR1 of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 585. Claims 1,3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer

comprising assaying an obtained sample with antibody binding to VEGFR1, classified in Class 435, subclass 7.1

Group 586-651. Claims 1-3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells comprising assaying an obtained sample with antibody binding to VEGFR1 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGFR1 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 652. Claims 1,3 and 4 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of VEGFR1 in an immunoassay, in an obtained sample, with antibody binding to VEGFR1, classified in Class 435, subclass 7.1

Group 653-716. Claims 1-3 and 4, as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of VEGFR1 in an immunoassay, in an obtained sample, with antibody binding to VEGFR1 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial

expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGFR1 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 717. Claims 1,3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting VEGFR1, comprising assaying an obtained sample with antibody binding to VEGFR1 classified in Class 435, subclass 7.1

Group 718-781. Claims 1-3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting VEGFR1, comprising assaying an obtained sample with antibody binding to VEGFR1 and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGFR1 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

8. It is noted that claim 1 drawn to VEGF of the instant application has been determined to be a linking claim. The restriction requirement among the linked

inventions is subject to the nonallowance of the linking claim(s), claims 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 782. Claims 1,3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with antibody binding to VEGF, classified in Class 435, subclass 7.1

Group 783-846. Claims 1-3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells comprising assaying an obtained sample with antibody binding to VEGF and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or

2^6 in the instant case, the number of possible combinations, wherein VEGF must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 847. Claims 1,3 and 4 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of VEGF in an immunoassay, in an obtained sample, with antibody binding to VEGF, classified in Class 435, subclass 7.1

Group 848-911. Claims 1-3 and 4, as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of VEGF in an immunoassay, in an obtained sample, with antibody binding to VEGF and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGF must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 912. Claims 1,3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting VEGF, comprising

assaying an obtained sample with antibody binding to VEGF classified in Class 435, subclass 7.1

Group 913-976. Claims 1-3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting VEGF, comprising assaying an obtained sample with antibody binding to VEGF and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGF must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

9. It is noted that claim 1 drawn to bFGFR of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or

nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 977. Claims 1,3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with antibody binding to bFGFR, classified in Class 435, subclass 7.1

Group 978-1041. Claims 1-3 and 4, as it is drawn to a prediction of the existence of tamoxifen-resistant breast cancer, are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells comprising assaying an obtained sample with antibody binding to bFGFR and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein bFGFR must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1042. Claims 1,3 and 4 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of

bFGFR in an immunoassay, in an obtained sample, with antibody binding to bFGFR, classified in Class 435, subclass 7.1

Group 1043-1106. Claims 1-3 and 4, as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer, comprising detection of bFGFR in an immunoassay, in an obtained sample, with antibody binding to bFGFR and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein bFGFR F must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1107. Claims 1,3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting bFGFR, comprising assaying an obtained sample with antibody binding to bFGFR classified in Class 435, subclass 7.1

Group 1108-1171. Claims 1-3 and 5 as it is drawn to a method of determining survival for an individual with breast cancer by detecting bFGFR, comprising assaying an obtained sample with antibody binding to bFGFR and one or more of the additional six polypeptides recited in claim 1 section b), classified in Class 435, subclass 7.1. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible

combinations, wherein bFGFR must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

10. It is noted that claim 6 drawn to TIE-2 of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 6. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 1172. Claims 6 and 8 drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify TIE-2, classified in Class 435, subclass 6.

Group 1173-1236. Claims 6-8 are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify TIE-2 and one or more pairs of primers of the additional six nucleic acids recited in claim 6 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TIE-2 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of nucleic acids for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1237. Claims 6, 9 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, and subsequent patient survival comprising detection of TIE-2, in an amplification assay, in an obtained sample, with a pair of primers to TIE-2, classified in Class 435, subclass 6.

Group 1238-1301. Claims 6, 7, 9 as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer and subsequent patient survival, comprising detection of TIE-2 in an amplification assay, in an obtained sample, with a pair of primers binding to TIE-2 and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TIE-2 must be part of the group is 64. Each of the combinations is a

separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1302. Claims 6, 10 are drawn to determining survival for an individual with breast cancer comprising detection of TIE-2, in an amplification assay, in an obtained sample, with a pair of primers to TIE-2, classified in Class 435, subclass 6.

Group 1303-1366. Claims 6, 7, 10 are drawn to determining survival for an individual with breast cancer, comprising detection of TIE-2 in an amplification assay, in an obtained sample, with a pair of primers binding to TIE-2 and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TIE-2 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

11. It is noted that claim 6 drawn to EDNRA of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 6. Upon the allowance of the linking claim(s), the restriction requirement as to the linked

inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 1367. Claims 6 and 8 drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify EDNRA, classified in Class 435, subclass 6.

Group 1368-1432. Claims 6-8 are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify EDNRA and one or more pairs of primers of the additional six nucleic acids recited in claim 6 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein EDNRA must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of nucleic acids for

examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1433. Claims 6, 9 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, and subsequent patient survival comprising detection of EDNRA, in an amplification assay, in an obtained sample, with a pair of primers to EDNRA, classified in Class 435, subclass 6.

Group 1434-1497. Claims 6, 7, 9 as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer and subsequent patient survival, comprising detection of EDNRA in an amplification assay, in an obtained sample, with a pair of primers binding to EDNRA and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein EDNRA must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1498. Claims 6, 10 are drawn to determining survival for an individual with breast cancer comprising detection of EDNRA, in an amplification assay, in an obtained sample, with a pair of primers to EDNRA, classified in Class 435, subclass 6.

Group 1499-1562. Claims 6, 7, 10 are drawn to determining survival for an individual with breast cancer, comprising detection of EDNRA in an amplification assay, in an obtained sample, with a pair of primers binding to EDNRA and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein EDNRA must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

12. It is noted that claim 6 drawn to TGF beta 3 of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 6. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are

no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 1563. Claims 6 and 8 drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify TGF beta 3, classified in Class 435, subclass 6.

Group 1564-1628. Claims 6-8 are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify TGF beta 3 and one or more pairs of primers of the additional six nucleic acids recited in claim 6 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGF beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of nucleic acids for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1629. Claims 6, 9 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, and subsequent patient survival comprising detection of TGF beta 3, in an amplification assay, in an obtained sample, with a pair of primers to TGF beta 3, classified in Class 435, subclass 6.

Group 1630-1694. Claims 6, 7, 9 as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer and subsequent patient survival, comprising detection of TGF beta 3 in an amplification assay, in an obtained sample, with a pair of primers binding to TGF beta 3 and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGF beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1695. Claims 6, 10 are drawn to determining survival for an individual with breast cancer comprising detection of TGF beta 3, in an amplification assay, in an obtained sample, with a pair of primers to TGF beta 3, classified in Class 435, subclass 6.

Group 1696-1758. Claims 6, 7, 10 are drawn to determining survival for an individual with breast cancer, comprising detection of TGF beta 3 in an amplification assay, in an obtained sample, with a pair of primers binding to TGF beta 3 and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGF beta 3 must be part of the

group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

13. It is noted that claim 6 drawn to TGFR beta 3 of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 6. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 1759. Claims 6 and 8 drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify TGFR beta 3, classified in Class 435, subclass 6.

Group 1760-1824. Claims 6-8 are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify TGFR beta 3 and one or more pairs of primers of the additional six nucleic acids recited in claim 6 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGFR beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of nucleic acids for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1825. Claims 6, 9 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, and subsequent patient survival comprising detection of TGFR beta 3, in an amplification assay, in an obtained sample, with a pair of primers to TGFR beta 3, classified in Class 435, subclass 6.

Group 1826-1889. Claims 6, 7, 9 as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer and subsequent patient survival, comprising detection of TGFR beta 3 in an amplification assay, in an obtained sample, with a pair of primers binding to TGFR beta 3 and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible

combinations, wherein TGFR beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 1890. Claims 6, 10 are drawn to determining survival for an individual with breast cancer comprising detection of TGFR beta 3, in an amplification assay, in an obtained sample, with a pair of primers to TGFR beta 3, classified in Class 435, subclass 6.

Group 1891-1954. Claims 6, 7, 10 are drawn to determining survival for an individual with breast cancer, comprising detection of TGFR beta 3 in an amplification assay, in an obtained sample, with a pair of primers binding to TGFR beta 3 and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein TGFR beta 3 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

14. It is noted that claim 6 drawn to VEGFR1 of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 6. Upon the

allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 1955. Claims 6 and 8 drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify VEGFR1, classified in Class 435, subclass 6.

Group 1956-2020. Claims 6-8 are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify VEGFR1 and one or more pairs of primers of the additional six nucleic acids recited in claim 6 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGFR1 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is

required to elect and specify a single combination of nucleic acids for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 2021. Claims 6, 9 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, and subsequent patient survival comprising detection of VEGFR1, in an amplification assay, in an obtained sample, with a pair of primers to VEGFR1, classified in Class 435, subclass 6.

Group 2022-2085. Claims 6, 7, 9 as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer and subsequent patient survival, comprising detection of VEGFR1 in an amplification assay, in an obtained sample, with a pair of primers binding to VEGFR1 and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGFR1 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 2086. Claims 6, 10 are drawn to determining survival for an individual with breast cancer comprising detection of VEGFR1, in an

amplification assay, in an obtained sample, with a pair of primers to VEGFR1, classified in Class 435, subclass 6.

Group 2087-2151. Claims 6, 7, 10 are drawn to determining survival for an individual with breast cancer, comprising detection of VEGFR1 in an amplification assay, in an obtained sample, with a pair of primers binding to VEGFR1 and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGFR1 must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

15. It is noted that claim 6 drawn to VEGF of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 6. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or

nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 2152. Claims 6 and 8 drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify VEGF, classified in Class 435, subclass 6.

Group 2153-2217. Claims 6-8 are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify VEGF and one or more pairs of primers of the additional six nucleic acids recited in claim 6 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGF must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of nucleic acids for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 2218. Claims 6, 9 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, and subsequent patient survival comprising detection of VEGF, in an amplification assay, in an obtained sample, with a pair of primers to VEGF, classified in Class 435, subclass 6.

Group 2219-2283. Claims 6, 7, 9 as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer and subsequent patient survival, comprising detection of VEGF in an amplification assay, in an obtained sample, with a pair of primers binding to VEGF and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGF must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 2284. Claims 6, 10 are drawn to determining survival for an individual with breast cancer comprising detection of VEGF, in an amplification assay, in an obtained sample, with a pair of primers to VEGF, classified in Class 435, subclass 6.

Group 2285-2349 Claims 6, 7, 10 are drawn to determining survival for an individual with breast cancer, comprising detection of VEGF in an amplification assay, in an obtained sample, with a pair of primers binding to VEGF and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein VEGF must be part of the group is 64. Each

of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

16. It is noted that claim 6 drawn to bFGFR of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 6. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 2350. Claims 6 and 8 drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify bFGFR, classified in Class 435, subclass 6.

Group 2351-2415. Claims 6-8 are drawn to a method for detecting/diagnosing tamoxifen-resistant breast cancer cells/cancer comprising assaying an obtained sample with a pair of primers to amplify bFGFR and one or more pairs of primers of the additional six nucleic acids recited in claim 6 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein bFGFR must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of nucleic acids for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 2416. Claims 6, 9 are drawn to a prediction of the development of tamoxifen-resistant breast cancer, and subsequent patient survival comprising detection of bFGFR, in an amplification assay, in an obtained sample, with a pair of primers to bFGFR, classified in Class 435, subclass 6.

Group 2417-2481. Claims 6, 7, 9 as it is drawn to a prediction of the development of tamoxifen-resistant breast cancer and subsequent patient survival, comprising detection of bFGFR in an amplification assay, in an obtained sample, with a pair of primers binding to BFGFR and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein bFGFR must be part of the group is 64. Each of the combinations is

a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 2482. Claims 6, 10 are drawn to determining survival for an individual with breast cancer comprising detection of bFGFR, in an amplification assay, in an obtained sample, with a pair of primers to bFGFR, classified in Class 435, subclass 6.

Group 2483-2547 Claims 6, 7, 10 are drawn to determining survival for an individual with breast cancer, comprising detection of BFGFR in an amplification assay, in an obtained sample, with a pair of primers binding to bFGFR and one or more pairs of primers of the additional six nucleic acids recited in claim 1 section b), classified in Class 435, subclass 6. It is noted that by binomial expansion, that is 2^{n-1} or 2^6 in the instant case, the number of possible combinations, wherein bFGFR must be part of the group is 64. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of polypeptides for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group 2548. Claim 11 is drawn to a method for altering the phenotype of a breast cancer cell comprising contacting the cell with a TIE-2 gene and a promoter classified in Class 435, subclass 6.

Group 2549. Claim 11 is drawn to a method for altering the phenotype of a breast cancer cell comprising contacting the cell with a EDNRA gene and a promoter classified in Class 435, subclass 6.

Group 2550. Claim 11 is drawn to a method for altering the phenotype of a breast cancer cell comprising contacting the cell with a TGR beta 3 gene and a promoter classified in Class 435, subclass 6.

Group 2551. Claim 11 is drawn to a method for altering the phenotype of a breast cancer cell comprising contacting the cell with a TGFR beta 3 gene and a promoter classified in Class 435, subclass 6.

Group 2552. Claim 11 is drawn to a method for altering the phenotype of a breast cancer cell comprising contacting the cell with a VEGFR1 and a promoter classified in Class 435, subclass 6.

Group 2553. Claim 11 is drawn to a method for altering the phenotype of a breast cancer cell comprising contacting the cell with a VEGF gene and a promoter classified in Class 435, subclass 6.

Group 2554. Claim 11 is drawn to a method for altering the phenotype of a breast cancer cell comprising contacting the cell with a bFGFR gene and a promoter classified in Class 435, subclass 6.

17. It is noted that claim 12 of the instant application has been determined to be a linking claim. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 12. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the

limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 2555. Claims 12 and 13 are drawn to a method for treating breast cancer comprising providing an effective amount of an antiangiogenic agent, AGM-1470 (TNP-470) and tamoxifen classified in Class 512, subclass 2+.

Group 2556. Claims 12 and 13 are drawn to a method for treating breast cancer comprising providing an effective amount of an antiangiogenic agent, platelet factor 4 and tamoxifen classified in Class 512, subclass 2+.

Group 2557. Claims 12 and 13 are drawn to a method for treating breast cancer comprising providing an effective amount of an antiangiogenic agent, angiostatin and tamoxifen classified in Class 512, subclass 2+.

Group 2558. Claim 14 is drawn to a method for treating breast cancer comprising providing an effective amount of an antisense construct containing a TIE-2 gene classified in Class 514, subclass 44.

Group 2559. Claim 14 is drawn to a method for treating breast cancer comprising providing an effective amount of an antisense construct containing a EDNRA gene classified in Class 514, subclass 44.

Group 2560. Claim 14 is drawn to a method for treating breast cancer comprising providing an effective amount of an antisense construct containing a TGF beta 3 gene classified in Class 514, subclass 44.

Group 2561. Claim 14 is drawn to a method for treating breast cancer comprising providing an effective amount of an antisense construct containing a TGFR beta 3 gene classified in Class 514, subclass 44.

Group 2562. Claim 14 is drawn to a method for treating breast cancer comprising providing an effective amount of an antisense construct containing a VEGFR1 gene classified in Class 514, subclass 44.

Group 2563. Claim 14 is drawn to a method for treating breast cancer comprising providing an effective amount of an antisense construct containing a VEGF gene classified in Class 514, subclass 44.

Group 2564. Claim 14 is drawn to a method for treating breast cancer comprising providing an effective amount of an antisense construct containing a bFGFR gene classified in Class 514, subclass 44.

Group 2565. Claim 15 is drawn to a method for treating breast cancer comprising providing an effective amount of an expression construct containing a gene encoding bFGFR classified in Class 514, subclass 44.

Group 2566-7606. Claim 16 is drawn to a kit comprising one or more antibodies that specifically bind to seven different polypeptides. It is noted

that by Factorial Analysis, claim 16 is drawn to 5040 separate and distinct inventions. The invention is classified in Class 530, subclass 387.1 and 389.1. Applicant is required to elect and specify a single combination of antibodies in a kit for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species.**

Group 7606-12646. Claim 17 is drawn to a kit comprising one or more pairs of primers effective to amplify one or more of seven different polynucleotides. It is noted that by Factorial Analysis, claim 16 is drawn to 5040 separate and distinct inventions. The invention is classified in Class 536, subclass 23.1. Applicant is required to elect and specify a single combination of antibodies for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species.**

Group 12647. Claim 18 is drawn to a method for detecting markers for tamoxifen-resistant breast cancer comprising isolating and screening nucleic acids classified in Class 435, subclass 6.

Group12648-12733. Claims 19-20 are drawn to a pharmaceutical composition comprising two or more nucleic acids selected from the group consisting of the seven nucleic acids claimed in claim 19, wherein said nucleic acids are in the form of vectors, classified in Class 536, subclass 23.1, and Class 435, subclass 320.1. Applicants have correctly stated on page 6 of the response that the proper analysis of this claim set is 85 combinations. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of nucleic acids for

examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

Group12734-12818. Claim 21 is drawn to a pharmaceutical composition comprising two or more polypeptides selected from the group consisting of the seven polypeptides claimed in claim, classified in Class 530, subclass 350+ and Class 514, subclass 2+. Applicants have correctly stated on page 6 of the response that the proper analysis of this claim set is 85 combinations. Each of the combinations is a separate and distinct invention. Applicant is required to elect and specify a single combination of nucleic acids for examination. **It is noted for Applicant's convenience that the instant requirement is not an election of species requirement.**

18. The inventions are distinct, each from the other because of the following reasons:

Inventions of the Groups 2566-12646/12648-12733 as disclosed are biologically and chemically distinct, made by and used in different methods and are therefore distinct inventions.

Inventions of the Groups of Group 1172-2565/12647 are materially distinct methods which differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success.

The inventions of Groups 2566-7606/12734-12818 and 1-1171 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (I) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as

claimed can be used in a materially different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case the antibody products as claimed and the polypeptide products as claimed can be used in materially different processes such as production of anti-idiotypic antibodies and production of antibodies, respectively.

The inventions of Groups 7606-12646/12647-12733 and 1172-2554.2558-2565.12647 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (I) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case the nucleic acid products as claimed can be used in materially different processes such synthesis of polypeptides and fragments of polypeptides for the production of antibodies.

The inventions of the Groups of Groups 2555-2557 and 2566-12646/12648-12818 are not at all related because the antibody, polypeptides, nucleic acids of Groups 2566-12646/12648-12818 are not used in any of the methods of 2555-2557.

The inventions of Groups 2566-7606/12734-12818 and Groups 1172-2554/2558-2565/12647 are not at all related because the antibodies/polypeptides of the Groups 2566-7606/12734-12818 are not used in any of the methods of 1172-2554/2558-2565/12647.

The inventions of Groups 7606-12646/12648-12733 and Groups 1-1171 are not at all related because the nucleic acids of the Groups 7606-12646/12648-12733 are not used in any of the methods of Groups 1-1171

19. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and/or recognized divergent subject matter, restriction for examination purposes as indicated is proper.

20. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

22. Some of Applicants traverse of the previous restriction requirement is relevant to the instant restriction requirement.

Applicant argues that claims 1, 2, 7, 16, 17, 19-21 comprise generic linking claims and are in proper Markush format as is claim 12 and state that restriction of linking claims and Markush claims is improper. The argument has been considered

but has not been found proper because although claims 1, 2, 7, 16, 17, 19 and 21 are Markush groups, claims 12 and 20 are not Markush groups. In addition, claims 16 and 17 are not generic linking claim, but rather are Markush groups. Further, claims 1 and 6 not only recite Markush groups, but also are linking claims, as is claim 12. It is noted that Examiner has redrawn the restriction requirement to reflect the groups linked to claims 1, 6 and 12. Linking claim restriction is proper. Further, as drawn to the restriction of the Markush groups, each of the restricted groups is drawn to distinct inventions which are not obvious one over the over. Although Applicant appears to argue that the members of the Markush group share common utilities and therefore have unity of invention, MPEP 803.02 specifically requires that unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility. Although Applicant points to MPEP 803.02 to argue that a provisional election of a single species, rather than a restriction to a separate invention may be required, a review of the example wherein this is applicable to generic Markush-type claims reveals that in this is meant to apply claims drawn to, for example, "compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE." It is clear that a substantial structural feature is here disclosed as being essential to the utility.

22. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Susan Ungar
Primary Patent Examiner
June 29, 2003